Highlander → 512 536 3184

1. --A method for increasing viral vector infection of epithelial cells in an epithelial tissue comprising:

a) contacting said epithelial tissue with a composition that comprises a hypotonic solution and/or a chelator of divalent cations in an amount sufficient to produce permeabilized epithelial tissue; and

b) contacting said permeabilized epithelial tissue with a viral vector;

whereby an increase in transepithelial permeability increases viral vector infection of said epithelial cells.--

Hypotonic shock ↑ transepithelial perm. p4/5 L24 → Necessity for chelator

2. (Currently amended) The method of claim 1, wherein said epithelial ~~tissue is~~ cells are in airway epithelial tissue.

3. (Currently amended) The method of claim 2, wherein said airway epithelial tissue is bronchial or bronchiolar tissue.

4. (Original claim) The method of claim 2, wherein said airway epithelial tissue is tracheal tissue.

5. (Original claim) The method of claim 2, wherein said airway epithelial tissue is alveolar tissue.

6. (Original claim) The method of claim 1, further comprising increasing the proliferation of said epithelial cells.

7. (Original claim) The method of claim 6, wherein increasing the proliferation of said epithelial cells is achieved by contacting said cells with a proliferative factor.

8. (Original claim) The method of claim 7, wherein said proliferative factor is a growth factor.

9. Canceled in A

10. (Currently amended) The method of claim 91, wherein said ~~tissue permeabilizing agent~~ composition is a hypotonic solution.

11. (Currently amended) The method of claim 91, wherein said ~~tissue permeabilizing agent is an ion chelator.~~ composition comprises a chelator of divalent cations.

12. (Original claim) The method of claim 11, wherein said ~~ion chelator~~ chelator of divalent cations is EGTA, BAPTA or EDTA.

13-25. (Canceled)

26. (Currently amended) The method of claim 1, further comprising, ~~following the step of increasing transepithelial permeability,~~ infecting said epithelial ~~tissue~~ cells with a virus vector selected from the group consisting of a retrovirus, a lentivirus, an adenovirus, an adeno-associated virus, a parvovirus, a papovavirus, paramyxovirus and a vaccinia virus.

27. (Original claim) The method of claim 26, wherein the virus vector comprises a non-viral gene under the control of a promoter active in eukaryotic cells.

28. (Original claim) The method of claim 27, wherein said non-viral gene is a human gene.

29. (Original claim) The method of claim 28, wherein said gene encodes a polypeptide selected from the group consisting of a tumor suppressor, a cytokine, an enzyme, a toxin, a growth factor, a membrane channel, an inducer of apoptosis, a transcription factor, a hormone and a single chain antibody.

30. (Original claim) The method of claim 26, wherein the virus vector is a replication-defective virus.

31. (Original claim) The method of claim 30, wherein the virus vector is a retroviral vector.

32. (Original claim) The method of claim 1, wherein said epithelial tissue is diseased.

33. (Original claim) The method of claim 32, wherein said disease is lung cancer, tracheal cancer, asthma, surfactant protein B deficiency, alpha-1-antitrypsin deficiency or cystic fibrosis.

34. (Original claim) The method of claim 7, wherein said proliferative factor is delivered as an aerosol.

35. (Original claim) The method of claim 7, wherein said proliferative factor is delivered as a topical solution.

36. (Currently amended) The method of claim 91, wherein said ~~tissue permeabilizing agent~~ is delivered as an aerosol.

37. (Currently amended) The method of claim 91, wherein said ~~tissue permeabilizing agent~~ is delivered as a topical solution.

38-39. (Canceled)

41-47. (Canceled)

48. (Currently amended) A *in vivo* method for redistributing viral receptors on an epithelial ~~cells~~ cell of an epithelial tissue from the basolateral side to the apical side of said epithelial cell comprising increasing the transepithelial permeability of said epithelial tissue by contacting said epithelial tissue with a hypotonic solution and/or ~~an ion chelator~~, whereby increased transepithelial permeability facilitates redistribution of said viral receptors on said epithelial ~~cells~~ cell.

49. (Original claim) The method of claim 48, wherein said receptor is a retroviral receptor.

50. (Currently amended) A method for expressing a polypeptide in cells of an epithelial tissue comprising:

(a) providing a packaged viral vector comprising a polynucleotide encoding said polypeptide;

(b) increasing the permeability of said epithelial tissue by treating said tissue with a hypotonic solution and/or ~~an ion chelator~~ a chelator of divalent cations; and

(c) contacting cells of ~~said~~ the permeabilized epithelial tissue with said packaged viral vector under conditions permitting the uptake of said packaged viral vector by said cells and expression of said polypeptide therein;

whereby increased permeability of said epithelial tissue facilitates improved viral transduction of said cells, which in turn facilitates expression of said polypeptide.

51. (Original claim) The method of claim 50, further comprising increasing the proliferation of cells of said epithelial tissue.

53 --A method of increasing [illegible] chloride ions in airway epithelial tissue of a mammal suffering from cystic fibrosis comprising:

a) providing a packaged viral vector comprising a polynucleotide encoding a cystic fibrosis transmembrane regulator (CFTR) protein;

b) contacting said airway epithelial tissue with a hypotonic solution and/or a chelator of divalent cations in a sufficient amount to produce permeabilized epithelial tissue; and

c) contacting cells of said permeabilized airway epithelial tissue with said packaged viral vector under conditions permitting uptake of the packaged viral vector by said cells, and expression of said CFTR protein therein;

wherein a sufficient quantity of said CFTR protein is produced to increase chloride ion transport in the airway epithelial tissue.--

permeabilized airway

(c) contacting cells of said epithelial tissue with said packaged viral vector under conditions permitting the uptake of said packaged viral vector by said cells and expression of said ~~therapeutic polypeptide~~ CFTR protein therein,

~~whereby expression of said therapeutic polypeptide treats said disease CFTR protein provides said CFTR protein to said epithelial tissue.~~ wherein a sufficient quantity of said CFTR protein is produced to increase chloride ion transport in the airway epithelial tissue.

54. (Currently amended) The method of claim 53, further comprising increasing the proliferation of cells of said ~~diseased~~ epithelial tissue.

55. (Canceled)

56. (Currently amended) The method of claim ~~55~~53, wherein said ~~diseased~~ airway tissue is alveolar tissue, bronchial tissue or tracheal tissue.

57-65. (Canceled)

66. (Original claim) The method of claim 54, wherein increasing the proliferation of cells of said diseased epithelial tissue comprises contacting said cells with a proliferative agent.

67. (Original claim) The method of claim 53, wherein said viral vector is a retroviral vector.

68. (Canceled)

69. (Canceled)

70. (Currently amended) A method for ~~transforming~~ transducing epithelial cells with a viral vector comprising delivering to said epithelial cells a packaged viral vector and EGTA in a hypotonic solution.

11/22/04